SECOND EDITION

IMMUNOLOGY

JANIS KUBY

Cover credits
Background: lymph node macrophage attached to an endothelial cell.

Inset: X-ray crystallography of a peptide bound to a human class II MHC molecule, DR1.
Courtesy of J. H. Brown, 1993, *Nature* 364:33.

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Adoptive-Transfer Systems

In some cases it is important to eliminate the immune responsiveness of the syngeneic host so that the response of only the transferred lymphocytes can be studied in isolation. In adoptive-transfer systems the immune cells of the syngeneic recipient are inactivated by exposing the host to x-rays. Subjecting a mouse that will serve as host to sublethal doses of x-rays (650–750 rads) can kill 99.99% of its lymphocytes, after which the lymphocytes from the spleen of a syngeneic donor can be studied without interference from host lymphocytes. If the host's hematopoietic cells might influence an adoptive-transfer experiment, then higher x-ray levels (900–1000 rads) are used to eliminate the entire hematopoietic system. Mice irradiated with such doses will die unless reconstituted with bone marrow from a syngeneic donor.

The adoptive-transfer system has enabled immunologists to study the development of injected lymphoid stem cells in various organs of the recipient. Adoptive-transfer experiments have also facilitated the study of various populations of lymphocytes and of the cellular interactions required to generate an immune response. For example, it was through such experiments that immunologists were first able to show that a T helper cell is necessary for B-cell activation in the humoral response.

Scid Mice and *Scid*-Human Mice

An autosomal recessive mutation resulting in severe combined immunodeficiency disease (scid) developed spontaneously in a strain of mice called CB-17. These CB-17 *scid* mice fail to develop mature T and B cells and consequently are severely compromised immunologically. The mechanism of the defect in these mice has been determined and is discussed in Chapter 8. *Scid* mice must be housed in a sterile (germfree) environment if they are to survive, since they cannot fight off microorganisms of even low pathogenicity. The absence of functional T and B cells enables these mice to accept foreign cells and grafts from other strains of mice or even from other species. Apart from their lack of functional T and B cells, *scid* mice appear to be normal in all respects. When normal bone marrow cells are injected into *scid* mice, normal T and B cells develop, and the mice are cured of their immunodeficiency. This finding has made *scid* mice a valuable model system for the study of immunodeficiency and the process of differentiation of bone-marrow stem cells into mature T or B cells.

Interest in *scid* mice has mushroomed recently with the development of a new way to utilize them to study the human immune system. Implantation in *scid* mice of portions of human fetal liver, thymus, and lymph nodes causes the mice to become populated with mature human T and B lymphocytes (Figure 2-1). Because the mice lack mature T and B cells of their own, they do not reject the transplanted human tissue. The fetal liver contains immature human blood cells, including lymphocytes, and these immature cells mature into T and B cells within the human tissue implants. Because the human lymphocytes are exposed to mouse antigens while they are still immature, they later recognize mouse cells as self and do not mount an immunologic response against the mouse host. The beauty of this system is that it enables one to study human lymphocytes within an animal model. As will become apparent in later chapters, the *scid*-human mouse has become a valuable animal model that has been used to study development of various lymphoid cells and has also served as an important animal model in AIDS research. There are, however, important ethical considerations that must be addressed concerning the use of human fetal tissue in research.

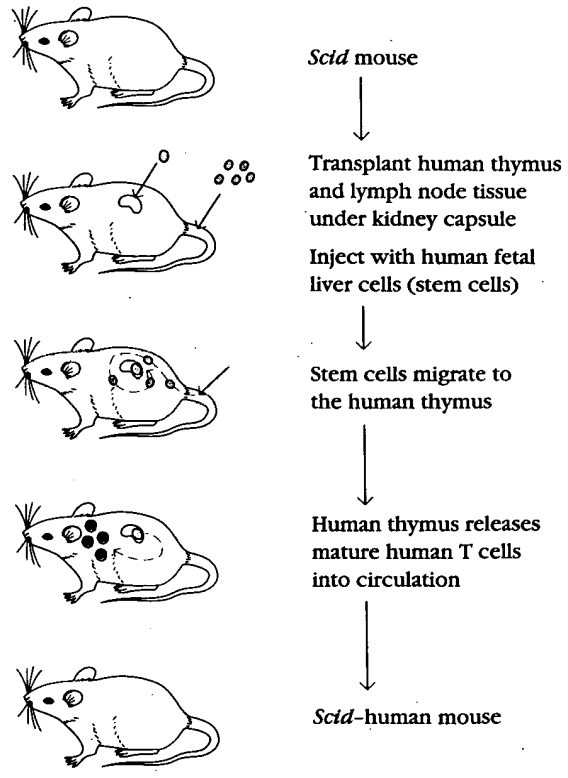

FIGURE 2-1 Production of *scid*-human mouse. This system permits study of human lymphocytes within an animal model.